UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/678,414	10/02/2003	Lawrence M. Kauvar	388512010101	9986

25225 7590 05/18/2007
MORRISON & FOERSTER LLP
12531 HIGH BLUFF DRIVE
SUITE 100
SAN DIEGO, CA 92130-2040

EXAMINER	
WESSENDORF, TERESA D	
ART UNIT	**PAPER NUMBER**
1639	
MAIL DATE	**DELIVERY MODE**
05/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/678,414	KAUVAR ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *2/27/07*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *43-51* is/are pending in the application.

4a) Of the above claim(s) *48 and 49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *43-47,50 and 51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 43-51 are pending

Claims 48 and 49 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species.

Claims 43-47 and 50-51 are under examination.

Withdrawn Rejection

In view of the amendments to the claims and applicant's arguments the rejections of the claims under 35 USC 102 is withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 50 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time

the application was filed, had possession of the claimed invention. (This is a new matter rejection).

Claim 50, which recites "a multiplicity" of a particulate different label is not supported in the as-filed specification. MPEP 714.02 clearly states that applicants point out where in the specification support for the new limitations appear in the original disclosure.

Double Patenting

In view of the terminal disclaimer on the record, the obviousness double patenting rejection is withdrawn.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 50-51, as amended, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Only the remaining rejections are reiterated below.

2. It is not clear how a spatial arrangement of a multiplicity of particulate different label in claim 50 differs

from the particulate label of claim 43 that makes the components of claim 43 different.

Response to Arguments

Applicants state that claim 43 requires only a single particulate label; claim 50 requires an arrangement of a multiplicity of different particulate labels and they must be spatially arranged so that they can be separately identified.

In reply, if claim 43 is only a single particulate label then it is not clear as how it becomes a multiple particulate label. The metes and bounds of the multiplicity of the particulate of different labels and how such multiplicity is of such "spatially defined arrangement" are not clearly apparent from the claims or specification. It is not clear as to the number of multiple particulate and how the spatial arrangement of said multiple label in a defined manner is made. [The claim appears to broaden the base claim 43].

3. Claim 51 does not further limit claim 50 and is drawn to more a method rather than to the product with a positive identifying feature of the particulate label.

Response to Arguments

Applicants state that claim 51 further limits claim 50 because the spatial arrangement must be on a surface - not within a three-dimensional volume.

In response, applicants' argument does not address the issue that the claim appears to be more of a method claim. The claim does not differentiate the difference between being displayed on a surface or three-dimensional volume. Furthermore, this is unclear since claim 50 neither recites displaying the particulate different labels on the surface or within a three-dimensional volume, as argued.

4. Claim 50, as amended, recites "each different particulate a different reagent" which is grammatically incorrect.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Rejections - 35 USC § 103

Claims 43-47 and 50-51, as amended, are rejected under 35 U.S.C. 103(a) as being unpatentable over Chee (USP 7,033,754)('754 patent) in view of Haughland (USP 5,719,031) or applicants' disclosure of known prior art for reasons of record and reiterated below.

Chee discloses at e.g., col. 9, lines 62 up to col. 32, line 25, a microspheres or beads or particles which is defined as a small discrete particles. The composition of the beads varies, depending on the class of bioactive agent. Suitable bead

compositions include those used in peptide e.g., latex. The bead sizes range from nanometers, i.e. 100 nm, to millimeters, i.e. 1 mm, with beads from about 0.2 micron to about 200 microns being preferred. In one embodiment, the DBL may be attached to a bead, i.e. a "decoder bead" that may carry a label such as a fluorophore. The use of multiple optical signatures increases the possible size of an array. In a preferred embodiment, the DBLs are either directly or indirectly labeled. By "labeled" is meant that a compound has at least one element, isotope or chemical compound attached to enable the detection of the compound. Examples of such labels include fluorophores. Decoding of self-assembled random arrays is done on the basis of pH titration. In this embodiment, in addition to bioactive agents, the beads comprise optical signatures, wherein the optical signatures are generated by the use of pH-responsive dyes (sometimes referred to herein as "pH dyes") such as fluorophores. This embodiment is similar to that outlined in PCT US98/05025 and U.S.S.N. 09/151,877, both of which are expressly incorporated by reference, except that the dyes used in the present invention exhibits changes in fluorescence intensity (or other properties) when the solution pH is adjusted from below the pKa to above the pKa (or vice versa). Each bead can contain any subset of the pH dyes, and in this way a unique code for the

bioactive agent is generated. In another preferred embodiment, a spatial or positional coding system is done. In this embodiment, there are sub-bundles or subarrays (i.e. portions of the total array) that are utilized. By analogy with the telephone system, each subarray is an "area code", that can have the same labels (i.e. telephone numbers) of other subarrays that are separated by virtue of the location of the subarray. Thus, for example, the same unique labels can be reused from bundle to bundle. Thus, the use of 50 unique labels in combination with 100 different subarrays can form an array of 5000 different bioactive agents. In this embodiment, it becomes important to be able to identify one bundle from another; in general, this is done either manually or through the use of marker beads; these can be beads containing unique tags for each subarray, or the use of the same marker bead in differing amounts, or the use of two or more marker beads in different ratios. There are additional ways to increase the number of unique or distinct tags. That is, the use of distinct attributes on each bead can be used to increase the number of codes. A variety of methods are used to generate a number of codes for use in the process of decoding the arrays, while minimizing the necessary decoding steps. For example, a variety of different coding strategies can be combined: thus, different "colors", combinations of colors

("hues"), different intensities of colors or hues or both, different colors and different bead sizes, etc. can all be combined. Alternatively, the number of distinct codes is markedly increased. In a preferred embodiment, the optical signature is generally a mixture of reporter dyes, preferably fluorescent. By varying both the composition of the mixture (i.e. the ratio of one dye to another) and the concentration of the dye (leading to differences in signal intensity), matrices of unique optical signatures may be generated. This may be done by covalently attaching the dyes to the surface of the beads. The dyes are preferably fluorescent dyes, which due to their strong signals provide a good signal-to-noise ratio for decoding. The encoding can be accomplished in a ratio of at least two dyes, although more encoding dimensions may be added in the size of the beads, for example. In addition, the labels are distinguishable from one another; thus two different labels may comprise different molecules (i.e. two different fluors) or, alternatively, one label at two different concentrations or intensity. The dyes are covalently attached to the surface of the beads. This may be done as is generally outlined for the attachment of the bioactive agents, using functional groups on the surface of the beads. As will be appreciated by those in the art, these attachments are done to minimize the effect on the

dye. A population of oligonucleotides encoding a single DBL is labeled with a defined ratio of colors such that each bead to which the DBL binds is identified based on a characteristic "hue" formulated from the combination of the colored fluorophores. Two or three or more distinct dyes (colors) are available for use. In this instance the number of differentiable codes generated by labeling a population of oligonucleotides encoding a single DBL with any given color is three. However by allowing combinations of colors and color levels in the labeling, many more codes are generated. With four primary colors and two intensity levels (color is present or absent), fifteen different hues/stage are possible. If four dyes and three different intensity levels are used, then 73 different hues/stage are possible. In this case, acquisition of only 4 color images is sufficient to obtain information on 73 different coding hues. See further the Examples starting at col. 51, which describes the details of the microspheres or beads.

The Chee reference does not disclose the use of carboxamide as a linking agent. However Haughland discloses at col. 8, lines 1-10 that the covalent bond that attaches the dye to the polymer is selected to be generally resistant to spontaneous hydrolysis and also resistant to the degradation conditions being studied, e.g. to the action of the target enzyme(s); or, where required,

to acid or base. Typically the covalent bond between the dye and the polymer is a carboxamide, sulfonamide, ether or thioether but any bond between the dye that is chemically stable and resistant to the degradation conditions is suitable.

Applicants state at page 9,lines 5-16 that "..standard linking techniques applicable to a multiplicity of substances and to the functional groups available on particulate supports include…amide linkages generated from carboxyl and amino functional groups. Other examples ….are as set forth in the catalog…"

Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use carboxamide linkers in the support of Chee for the advantage taught by Haughland above. As recognized by applicants above, these linkers have been conventionally used in the art. One having ordinary skill in the art at the time of applicants' invention would be motivated to use carboxamide as a linker for the advantage taught by Haughland above, and its established used in the art as recognized by applicants' disclosure.

Response to Arguments

Applicants state the Chee patent('754) is not properly cited since the provisional application does not disclose

microspheres as small as 100 nm. The provisional application at page 10, beginning at line 30, describes bead sizes from 500 nm to millimeter size and a preferred lower dimension of 200 nm. What appears to be the corresponding portion in the issued patent, at column 10, specifies 100~nm/ml, unlike the provisional which specifies 500 nm/ml.

In reply, the provisional application of Chee at page 10, line 30 up to page 11, line 2 states that:

> The bead sizes range from ***nanometers***, i.e. 500 nm, to 1 millimeters, i.e. 1 mm, with beads from about 0.2 micron to about 200 microns being preferred, and from about 0.5 to about 5 micron being particularly preferred.

Thus, Chee positively recites that the bead range is in nanometer and provides only as an example a 500nm to 1 mm range but does not limit said nanometer diameter to said given example range of 500nm to 1mm.

The claims are not read in vacuum, rather in the light of the specification disclosure. Applicants' specification at e.g., page 8, line 8 similarly provides only a preferred range but does not seem to limit it to those recited therein:

> A preferred range is 100-***500***, preferably 100-300, and more preferably 100-200 nm diameter particles.

The Chee provisional application at e.g., page 28, lines 16-26:

> In alternative embodiments, additional encoding parameters can be added, such as microsphere size. For example, the use of different size beads may also allow the reuse of sets of unique tags; that is, it is possible to use ***microspheres of different sizes*** to expand the 20 encoding dimensions of the microspheres. Optical fiber arrays can be fabricated containing pixels with different fiber diameters, or same size diameters using different size beads. With different diameters, the largest wells can be filled with the largest microspheres and then moving onto progressively smaller microspheres in the smaller wells until all size wells are then filled. In this manner, the same dye ratio could be used to encode microspheres of 25 different sizes thereby expanding the number of different oligonucleotide sequences or chemical functionalities present in the array.

It would be within one having ordinary skill in the art to determine the optimum proportion i.e., to pick and choose the size in nanometer with a reasonable expectation of obtaining the claimed product. Chee's disclosure that the different size beads allows one to expand the 20 encoding dimensions of the microspheres would motivate one to optimize said size range. Determination of a result effective variable is well within one having ordinary skill in the art. Discovery of an optimum value is obvious engineering. In re Aller, 105 USPQ 233 (CCPA 1955).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this

action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

This application contains claims 48-49 drawn to a non-invention. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is(571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T. D. Wessendorf
Primary Examiner
Art Unit 1639

Tdw
May 9, 2007